

IN THE CLAIMS

Please amend the claims as follows:

1. (Currently Amended) A method of producing a lysosomal hydrolase with high mannose glycoprotein oligosaccharides comprising
  - a. introducing and expressing a polynucleotide encoding a glycoprotein lysosomal hydrolase into a mammalian cell;
  - b. culturing the mammalian cell in the presence of a lectin in an amount sufficient to obtain a lectin resistant mammalian cell;
  - c. isolating the lectin resistant mammalian cell;
  - d. culturing said lectin resistant mammalian cell in the presence of deoxymannojirimycin and kifunensine in an amount and for a time to inhibit glycosylation of the lysosomal hydrolase glycoprotein; and
  - e. collecting the lysosomal hydrolase with high mannose oligosaccharides glycoprotein.
2. (Original) The method of Claim 1, wherein said lectin is selected from the group consisting of ricin, concanavalin A, erthroglutinin, lymphoagglutinin, and wheat germ agglutinin.
3. (Original) The method of Claim 2, wherein said lectin is ricin.
4. (Cancelled).
5. (Currently Amended) The method of ~~Claim 4~~Claim 1, wherein said lysosomal hydrolase is selected from the group consisting of  $\alpha$ -glucosidase,  $\alpha$ -L-iduronidase,  $\alpha$ -galactosidase A, arylsulfatase, N-acetylgalactosamine-6-sulfatase, or  $\beta$ -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase,  $\beta$ -glucuronidase, Heparan N-sulfatase, N-Acetyl- $\alpha$ -glucosaminidase, ~~Acetyl-CoA- $\alpha$ -glucosaminide N-acetyl-transferase~~, N-acetyl-glucosamine-6 sulfatase, Galactose 6-

sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, ~~Arylsulfatase A~~  
~~Cerebroside~~, Ganglioside, Acid  $\beta$ -galactosidase ~~G<sub>M1</sub>-Ganglioside~~, Acid  $\beta$ -  
galactosidase, Hexosaminidase A, Hexosaminidase B,  $\alpha$ -fucosidase,  $\alpha$ -N-Acetyl  
galactosaminidase, Glycoprotein Neuraminidase, Aspartylglucosamine amidase, Acid  
Lipase, Acid Ceramidase, ~~Lysosomal Sphingomyelinase~~ and Sphingomyelinase.

6. (Currently Amended) The method of Claim 5, wherein said lysosomal hydrolase is ~~acid~~- $\alpha$ -glucosidase.
7. (Currently Amended) The method of Claim 1, further comprising contacting the collected ~~glycoprotein~~ lysosomal hydrolase with a N-acetylglucosamine-1-phosphotransferase (GlcNAc-phosphotransferase) comprising SEQ ID NO:2, SEQ ID NO:7, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:1, SEQ ID NO:3 or a combination thereof ~~GlcNAc-phosphotransferase~~.
8. (Original) The method of Claim 7, wherein the GlcNAc-phosphotransferase comprises SEQ ID NO:2.
9. (Original) The method of Claim 7, wherein the GlcNAc-phosphotransferase comprises SEQ ID NO:2 and SEQ ID NO:7.
10. (Original) The method of Claim 7, wherein the GlcNAc-phosphotransferase comprises SEQ ID NOS:4, 5 and 7.
11. (Currently Amended) The method of Claim 7, wherein the GlcNAc-phosphotransferase is encoded by a nucleotide sequence comprising SEQ ID NO:1 ~~or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:1.~~

12. (Currently Amended) The method of Claim 7, wherein the GlcNAc-phosphotransferase comprises an  $\alpha$ -subunit and a  $\beta$  subunit, which are encoded by a nucleotide sequence comprising SEQ ID NO:3 ~~or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:3~~; and a  $\gamma$  subunit, which is encoded by a nucleotide sequence comprising SEQ ID NO:6 ~~or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:6~~.
13. (Currently Amended) The method of Claim 7, further comprising purifying said glycoprotein lysosomal hydrolase after said contacting.
14. (Currently Amended) The method of Claim 7, wherein after said contacting with GlcNAc-phosphotransferase the method further comprises contacting with said glycoprotein lysosomal hydrolase with a N-acetylglucosamine-1-phosphodiester  $\alpha$ -N-Acetyl glucosaminidase (phosphodiester  $\alpha$ -GlcNAcase) comprising SEQ ID NO:18, SEQ ID NO:17 or a combination thereof phosphodiester  $\alpha$ -GlcNAcase.
15. (Original) The method of Claim 14, wherein said phosphodiester  $\alpha$ -GlcNAcase comprises an amino acid sequence of SEQ ID NO:18.
16. (Currently Amended) The method of Claim 14, wherein said phosphodiester  $\alpha$ -GlcNAcase is encoded by a nucleotide sequence comprising SEQ ID NO:17 ~~or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17~~.
17. (Currently Amended) The method of Claim 14, further comprising purifying said glycoprotein lysosomal hydrolase after said contacting.
18. (Original) The method of Claim 1, wherein said deoxymannojirimycin is present in an amount from about 0.1 mM to about 5.0mM.

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19. (Currently Amended) The method of Claim 1, wherein said kifunensine is ~~in~~ present in an amount from about 0.1  $\mu\text{g/ml}$  to about 10 $\mu\text{g/ml}$ .

Claims 20-65 (Cancelled).